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A New Method to Determine Volumetric Bone Mineral Density from Bi-Planar Dual Energy Radiographs Using a Finite Element Model: an Ex-Vivo Study

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Short title: VBMD Estimation from BP2E radiographs

Abstract

Finite element models (FEM) derived from QCT-scans were developed to evaluate vertebral strength but QCT scanners limitations are restrictive for routine osteoporotic diagnosis. A new approach considers using bi-planar dual energy (BP2E) X-rays absorptiometry to build vertebral FEM. The purpose was to propose a FEM based on BP2E absorptiometry and to compare the vertebral strength predicted from this model to a QCT-based FEM. Forty six vertebrae were QCT scanned and imaged with BP2E X-rays. Subject-specific vertebral geometry and bone material properties were obtained from both medical imaging techniques to build FEM for each vertebra. Vertebral body volumetric bone mineral density (vBMD) distribution and vertebral strength prediction from the BP2E-based FEM and the QCT-based FEM were compared. A statistical error of 7 mg/cm^3 with a RMSE of 9.6% and a R^2 of 0.83 were found in the vBMD distribution differences between the BP2E-based and qCT-based FEM. The average vertebral strength was 3321N ±1657 and 3768N ±1660 for the qCT-based and BP2E-based FEM respectively with a RMSE of 641N and R^2 of 0.92. This method was developed to estimate vBMD distribution in lumbar vertebrae from a pair of 2D-BMD images and demonstrated to be accurate to personalize the mechanical properties *in vitro.*

Keywords: Osteoporosis, bone mineral density, vertebral strength, bi-planar dual energy X-ray absorptiometry, finite element model

1. Introduction

Vertebral fractures are one of the most common clinical manifestations with the major adverse consequences of osteoporosis [9, 18]. Associated with pain, disability, mortality and impairment in the quality of life osteoporotic vertebral fractures affect 1.1% of women each year and 0.6% of men [3, 19]. Early diagnosis of patients with osteoporosis is essential to prevent vertebral fracture. However current diagnosis technique, such as dual-energy X-ray absorptiometry (DXA), can only predict 40 to 70 % of vertebral fractures [24]. Such method measures areal bone mineral density (aBMD) alone which does not account for vertebral geometry or the three dimensional (3D) distribution of the trabecular bone. One approach for improving fracture risk assessment is to estimate vertebral strength through Finite Element (FE) models with 3D geometry and mechanical properties derived from quantitative computed tomography (QCT) imaging [4, 6, 13, 21]. QCT-based FE models demonstrated good reliability in the vertebral strength prediction compared to *in vitro* experiments [4-6, 13, 16, 21] and demonstrated better results than DXA to prospectively assess the risk of new vertebral fractures in elderly men [27]. However, the main limitation of such approach in routine osteoporotic diagnosis is the high dose, time and cost of QCT-scanner. Alternative approach considers using low dose bi-planar dual energy (BP2E) X-rays absorptiometry to estimate volumetric Bone Mineral Density (vBMD) from aBMD images to implement in a FE model. This system allows for 3D reconstruction of the spine geometry [12] and measures aBMD in the sagittal and frontal plane [23] in a 2-minutes clinical examination.

The purpose of this study was to propose a FE model based on bi-planar dual energy absorptiometry and to compare the vertebral strength estimated from this model to a QCT-based FE model which is considered as a gold standard.

2. Material and methods

2.1 Specimens

Human bone samples were obtained from French body donation to science program (Laboratory of Anatomy, Faculty of Medicine Lyon Est, University of Lyon, France and Faculty of Medicine, Centre du don des corps, University Paris Descartes, France).

Fourteen lumbar spine segments from cadaveric specimens were considered in this study (9 females and 5 males, age 84 ±9 years). Donors were fresh cadavers and no exclusion criteria was specified. A total of 46 vertebrae were included (10 L1, 12 L2, 11 L3, 11 L4 and 2 L5), after exclusion of vertebrae anomalies found during radiological measurements and dissection (presence of particularly severe osteophytes, disc calcifications and previous vertebral fractures).

2.2 Data acquisition

QCT-scans of the vertebrae were performed on two systems depending on the origin of the spine sample. Eighteen vertebrae were scanned on a QCT machine (MX8000 IDT10, Philips Medical, Best, Netherlands), using the following settings; X-ray tube voltage and current: 120kV, 100mA, reconstruction matrix: 512×512, field of view: 250×250 mm, voxel size of 0.48×0.48×1 mm. They were scanned alongside a K2HPO4 phantom (Mindways, Austin, TX, USA). The remaining vertebrae were scanned on a Scanner ICT 256 (Philips Healthcare, Cleveland, OH, USA) with the following settings; X-ray tube voltage and current: 120kV, 1489mA/s, reconstruction matrix: 512×512, field of view: 250×250 mm, voxel size of 0.39×0.39×0.33 mm. A calibration phantom (QRM-ESP, QRM GmbH, Germany) was used to map gray scale values to bone mineral density. To ensure consistency between the different protocols and have a cross-calibration, the Mindways phantom was scanned alongside the European Spine Phantom to determine the HA concentration equivalent for the different parts of the Mindways phantom. Similar calibration was thus performed on the QCT images to measure vBMD in each vertebra.

Low dose bi-planar dual energy (BP2E) X-rays were acquired for all spine segments using a dual energy prototype of the EOS® system (EOS imaging, Paris, France) which can simultaneously take a pair of X-rays in the sagittal and frontal planes in upright position [8], allowing 3D reconstruction of the spine [12]. Two levels of energy can be achieved with the EOS prototype by quickly changing the X-ray tube settings between two fast scans (approximately 20 seconds depending on the size of the lumbar spine). Therefore the computed projected areal Bone Mineral Density (aBMD) images of the vertebrae are similar to DXA images [21, 23]. ABMD measurement was previously validated by comparing EOS accuracy and reproducibility with the dual x-ray absorptiometry densitometers' characteristics [23]. X-ray tube voltage and current were 140kV and 149mA for the high energy images and 70kV and 298mA for the low energy images.

2.3 Finite Element Models

A QCT-based finite element (FE) model was built from vertebral geometry obtained by a semi-automatic segmentation method [15]. A hexahedral mesh of the vertebra was generated from this geometry using a multiblock meshing program wrote in C++ [10]. Briefly, the multiblock meshing technique consists in multiple building blocks composed of meshing seeding arranged in rows, columns and layers. The mesh seeds are then projected on the vertebra surface and morphed to each vertebral surface as nodes to lay the foundation for the FE mesh [10], resulting to a different topology for each vertebral level. In this 17,000-element mesh the average element size was controlled to range between 1 mm and 1.5 mm. All FE meshes were generated with the same topology for each lumbar level allowing the same element to be located closely at the same position for each vertebra at the same lumbar level. Convergence analysis was performed to determine the ideal number of elements needed [26]. Once the mesh generated, the average BMD of a single finite element was defined on the basis of the QCT scan voxels that fall inside the element. A

volumetric BMD (vBMD) distribution was defined as the set of density values of each element of a model. As elements correspond to their counterpart in the same level vertebra mesh instances, comparison between vBMD distributions on element per element basis was feasible. Finally, vBMD values of the elements were converted to linear elastic mechanical properties from an experimental relationship between vBMD and elastic modulus [14] as shown in equation 1.

$$E\ (MPa) = 3230\ BMD\ (gHA/cm^3) - 34.7 \quad (1)$$

The Poisson ratio, ν, was set to 0.4 [13].

A bi-planar dual energy based (BP2E-based) FE model was built from vertebral geometry obtained by 3D reconstruction of the spine from bi-planar X-rays [12]. By using calibrated sagittal and frontal X-ray images we were able to reconstruct a patient-specific geometry of each vertebrae. FE meshes similar to the QCT-based model were generated using the same element numbering and topology.

The vBMD distribution was estimated for each mesh from the sagittal and/or frontal areal BMD (aBMD) images and a generic vBMD distribution, using the algorithm described in the following section. Finally, vBMD values were converted to material properties using the same equation 1.

2.4 vBMD distribution estimation from aBMD images

An algorithm was developed to estimate the vBMD distribution from bi-planar dual energy (BP2E) X-ray absorptiometry images for each vertebra. The global approach is illustrated in figure 1 and presented hereafter.

First, a database composed of the QCT-based FE mesh densities was built from the 46 vertebrae distinguishing each lumbar level. The database was composed of 10 L1, 12 L2, 11 L3, 11 L4 and 2 L5. From this database, a generic vBMD distribution was created by averaging for each single finite element the density found in all vertebrae for each lumbar level. By having the same topology

for all vertebral meshes we can obtain an initial FE mesh pre-filled with the generic vBMD distribution. Once we have an initial FE model filled with a generic vBMD distribution for a given vertebra, we were able to build digitally reconstructed radiographies (DRR) yielding to virtual aBMD images (frontal and sagittal views) based on the generic vBMD distribution. In this process, the vertebra under control was removed from the QCT-based FE mesh density database to not influence in the generic vBMD distribution. In order to personalize the vBMD distribution, these virtual aBMD images were compared to the BP2E aBMD images resulting from dual energy acquisition. Differences were quantified in terms of density value for each image pixel. Then, an automatic iterative adjustment of the vBMD distributions was performed to minimize these differences between the virtual and the BP2E aBMD images.

2.5 Boundary conditions

Previously described boundary conditions and failure criterion [21] were considered to compare the QCT-based and BP2E-based models. Briefly, each vertebra was virtually loaded in anterior compression via a thin layer of polymethyl-methacrylate (PMMA, about 0.5 to 1cm thick, E=2500 MPa, ν=0.3) placed over the vertebral endplates as performed previously [21]. Lower nodes of the lower PMMA layer were constrained in all degrees of freedom. Anterior compressive load was applied to a node located at the anterior third of the vertebra joined by rigid elements to the upper PMMA layer. Simulations were run on ANSYS software (ANSYS Inc., Canonsburg, PA, USA). The vertebral failure load was defined when a contiguous region of $1mm^3$ of elements reached 1.5% deformation as determined previously [21, 22].

2.6 Analysis of the accuracy of the predictive vBMD

The method developed to estimate the vBMD distribution from BP2E images can be affected by the number of radiography used (1 sagittal or 1 frontal or both radiographies). Therefore we first

compared the vBMD distribution from the QCT-based model, considered as a gold standard, to the BP2E-based model on 18 vertebrae with three methodologies to estimate the BP2E-based vBMD from the aBMD radiographies; 1) by using the sagittal radiography only, 2) by using the frontal radiography alone and 3) by using both radiographs. Once the best method was defined, the 46 vertebrae were used to validate the BP2E-based FEM from the qCT-based FEM by comparing the vertebral strength determined from each model.

In more details, one group composed of 18 vertebrae (from 5 donors, 4F and 1M, mean age: 78 ± 8 y.o.) was used to compare the vBMD distribution assessed by the QCT model to the three BP2E models (depending on the radiographies used for the method; 1) the sagittal image only, 2) the frontal image and 3) both frontal and sagittal BP2E images). To evaluate the vBMD estimation method, the mean BMD estimated in the vertebral body trabecular bone from each model was computed as the average of the inner vertebral body elements, weighted by each element volume. The two outer layers of elements, corresponding to cortical bone, were removed of the comparison as trabecular bone is more affected by osteoporosis than the cortical layer. Therefore the inner vBMD, corresponding to the trabecular bone, based from the BP2E model were compared to the average vBMD measured in the same volume on the qCT-based model. Each vertebra's centrum was then divided in 27 parts bounded by two frontal planes, two axial planes and two para-sagittal planes, as shown in figure 2.

This division of the vertebral body was performed to assess the reliability of the vBMD estimation method in different regions of the trabecular bone as regional variation is present in vertebral bone density [11]. Average vBMD distribution in each of the 27 regions based from the BP2E model were compared to the average vBMD measured in the same regions on the qCT-based model. The statistical error, the root mean square error (RMSE), Bland and Altman plots [2] and the non-

parametric Spearman R^2 coefficient between the vBMD estimated from each BP2E-based model and the vBMD measured from qCT-scan were computed. The statistical differences between the models were assessed by a Wilcoxon signed rank test ($p<0.05$).

The methodology presenting the least error and the highest R^2 coefficient was then applied to estimate the vBMD distribution on the BP2E-based FEM. Then, the vertebral strength calculated from both FEMs was determined on the 46 vertebrae as the maximum load the vertebrae can sustain before failure. Differences in vertebral strength between the BP2E-based FEM and qCT-based FEM were assessed by computing the standard error of the estimate (SEE), the RMSE and the parametric Pearson R^2 correlation coefficient. For both analysis the correlation coefficients (R^2) were calculated both in their raw and sample size adjusted forms (adj. R^2).

3. Results

3.1 Estimation of the vBMD

Three methodologies to estimate the vBMD distribution from the BP2E aBMD radiographies were compared to the QCT vBMD: 1) by using the sagittal radiography only, 2) by using the frontal view alone and 3) by using both radiographs. Results for the three methodologies are presented in Table 1 with Bland and Altman plots displayed in Figure 3.

The best method found to estimate the average vBMD from BP2E images with the lower RMSE was using the sagittal plane image alone which led to a RMSE of 10 mg/cm^3 compared to the qCT-based model. After dividing the vertebral body into 27 regions, the vBMD distribution of all regions were estimated with a RMSE of 13 mg/cm^3 using the sagittal radiograph. No significant vBMD distribution differences were found between the qCT-based model and the BP2E-based model.

3.2 Finite Element Model

The BP2E-based FE model vertebral strength was calculated using the sagittal radiograph only as it was established to be the method involving the lower errors in vBMD estimation. The mean vertebral strength estimated by the BP2E-based FE model and the QCT-based FE model were 3768 N ±1660 and 3321 N ±1657 respectively. A significant correlation coefficient was found between the two models with R^2 =0.92 with p<0.001 (adj. R^2=0.92 with p<0.001), a RMSE of 9.6 % and a Standard Error of the Estimate of 461 N (Figure 4 A-B).

4. Discussion

4.1 Distribution of the vBMD

The purpose of this study was to propose a new method to determine vBMD from bi-planar dual energy (BP2E) X-ray radiographies that could be used for osteoporotic vertebral strength estimation. First the technique used to build a vBMD distribution from BP2E X-rays was assessed by comparing the estimated vertebral body vBMD distribution to the measured vBMD from QCT scan. Second vertebral strength estimation was evaluated using a subject-specific Finite Element (FE) model built from the estimated BP2E vBMD compared to a QCT-based FE model considered as a gold standard.

Even though the 3D geometry of the spine was obtained by 3D reconstruction from the sagittal and frontal planes X-rays, three methodologies were analyzed to estimate the vBMD from the BP2E radiographies; 1) using the sagittal radiography only, 2) using the frontal view alone and 3) using both radiographs. Average vertebral body vBMD distribution from BP2E images showed a lower RMSE compared to qCT scan when using the sagittal plane radiograph alone to estimate vBMD with a 95% confidence interval (CI) of ± 20 mg/cm^3. The same conclusion was drawn when comparing vBMD in 27 sub-regions in the vertebral body. Using sagittal and frontal plane BP2E radiographs to estimate vBMD increased the RMSE of 48%. Using the frontal radiograph

alone increased the RMSE of 91%. This increase in error when using the frontal plane radiograph can be explained by the superimposition of the posterior arch with the vertebral body in the frontal view. With a mean density of 321 mg/cm^3 at the posterior arch vs 161 mg/cm^3 for the vertebral body, one can assume that the presence of the posterior elements in the frontal view can affect the estimation of the vertebral body's vBMD. For the same reasons, using the frontal view in addition to the sagittal view also deteriorated the average vertebral body vBMD.

This study is the first to report on the estimation vertebral body vBMD from the EOS BP2E X-rays. Previous studies used volumetric DXA (VXA) to determine vBMD distribution in the lumbar spine from L2 to L4 [29] and in the proximal femur [1, 28] and compared it with QCT vBMD. A statistical shape and density model was developed for L2, L3 and L4 to estimate vBMD from sagittal and frontal planes DXA images on female subjects [29]. Because this study explored VXA accuracy *in vivo*, which includes soft tissue artifact, the error found were higher than the present study with confidence intervals ranging from 41.2 to 51.8 mg/cm^3 in vertebral body vBMD estimation versus 20 mg/cm^3 in the present study. Their finding show great promises that using the EOS system *in vivo* could provide similar results. As for the femur, a 95% CI ranging from 40.8 mg/cm^3 to 56.2 mg/cm^3 were found in different region [28] which is higher than the present study (25 mg/cm^3 for the 27 regions). Correlation coefficient between 0.81 and 0.95 for the narrow neck [1] and the global proximal femur [28] were reported and the present study found correlation coefficients equal to 0.84. While the results cannot be compared directly because of the differences between DXA and EOS, the same range of correlations and vBMD estimation errors were found, which is encouraging for further study.

4.2 Finite Element Models

Vertebral strength estimation was also evaluated using a Finite Element (FEM) model built from the estimated BP2E vBMD compared to the QCT-based FEM. Some studies assessed vertebral strength prediction using a FE model based on QCT imaging [4-6, 13, 16]. The predicted ultimate force was well correlated with *in vitro* experiments with squared correlation coefficients ranging from 0.77 [5] to 0.95 [13]. Average reported vertebral strength varied between 2979 N to 5391 N which is in the range of the present results based on the qCT-based FEM (3321 N) and BP2E-based FEM (3768 N). A high significant squared correlation coefficient between the two models was found with a slope of 0.96 and an offset of 446 N meaning that the BP2E based model is a good predictor for vertebral strength estimation compared to the QCT-based FEM. One of the limitation is, the QCT-based FE model strength prediction accuracy was not examined with mechanically measured strength as *in vitro* experiments were not performed in the present study. However QCT based FEM is now a well-established method to determine vertebral strength [4-6, 13, 16], with future study will examine the accuracy of the models in estimating *in vitro* vertebral strength. Compared to DXA, which is the most used clinical tool to detect osteoporosis, FE models are more capable to predict vertebral strength. When considering *in vivo* study [27], DXA was fairly correlated to vertebral strength predicted from QCT-models with a correlation coefficient of 0.79. Moreover, FE strength was the most robust predictor for vertebral fracture prognostic compared to DXA. Therefore, FE models based on medical imaging would significantly help in predicting vertebral fractures. While QCT-based models present lots of advantages with volumetric geometry and BMD, they are also costly with high radiation dose required for moderately high-resolution. The present study could propose an alternative to the qCT scan disadvantages keeping volumetric geometry and BMD estimation possible. Indeed the EOS device is a low dose X-ray system with a fast acquisition time and an effective dose received of ~0.3 mSv

[7] compared to 5 mSv with qCT scan [27]. Sagittal and frontal DXA images were used with the same approach [1, 17, 20, 25, 30], however DXA images resolution is low with a high reproducibility error [1, 23, 28, 29] and the EOS system takes X-ray in a standing position so that postural influence on vertebral fracture can be assessed.

Provided the present model gives as good results *in vivo*, it would be a good alternative to QCT-based FE models. Several limitations are still to be considered. Possible error sources were the accuracy of the 3D reconstruction, which can affect the vertebral body volume and thus the apparent density, the contribution of the cortical bone layer and, to a lesser extent, the surrounding soft tissues. However, spine 3D reconstruction position precision was quantified to be less than 1.8 mm which should not affect average vBMD distribution [12]. Reproducibility of the volumetric BMD distribution from the EOS system was not assessed in the present study but areal BMD accuracy of the EOS system was determined to be below 5.2 per cent, versus 7.2 per cent for a DXA system in the same conditions [23]. As the transformation from aBMD into vBMD distribution is completely automated, we can assume that the accuracy will be similar than for the EOS aBMD. Cortical shell was not modeled in either FEMs since qCT-scan is not precise enough to measure cortical thickness with voxel sizes being larger than average cortical thickness in a vertebra. The influence of neglecting the cortical shell was not quantified in the present study but should be considered in future study including micro-CT imaging of the vertebrae. Thoracic vertebrae are also a concern for osteoporotic fractures, however L1 to L4 are easily measured in dual energy absorptiometry because of no superimposition of the thoracic cage or pelvis on the images.

Future studies should validate this model with *in vitro* experiments. The present study considered QCT-based FE models as gold standard but the literature [4-6, 13, 16] showed that an average

error ranging from 275 N to 1338 N can occur when comparing *in vitro* vertebral strength to QCT-based FE models predicted strength. Then the model should be validated *in vivo* considering soft tissue attenuation. Soft tissue characterization from the frontal view will allow for *in vivo* application.

This methodology was developed to estimate vBMD distribution in lumbar vertebrae from a pair of dual energy absorptiometry EOS images. This method is accurate enough and sufficient to personalize the mechanical properties in a FE model for vertebral strength estimation. Once these results are confirmed *in vivo*, FE models based on low dose bi-planar dual energy EOS images could become an alternative to QCT-based FEM.

Disclosures

The authors have no conflict of interest to declare. Wafa Skalli is the co-inventor of the EOS system without direct financial interest.

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Submission statement

We represent that this submission is original work, and is not under consideration for publication with any other journal

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Supporting information captions

Table 1: Mean (±SD), Root Mean Square Error (RMSE), the Spearman R^2 coefficient and the statistical error in volumetric bone mineral density distribution (vBMD) between the QCT scan model and the bi-planar dual energy (BP2E) model in the inner vertebral body and in the 27 trabecular regions as described in Figure 2 then pooled together before analysis.

vBMD (mg/cm^3)			**Sagittal view**	**Frontal view**	**Sagittal and Frontal views**
Inner body	Mean (SD)	qCT	124 (50)		
		BP2E	130 (45)	170 (46)	163 (50)
	RMSE (%)		10 (9.6%)	127 (91%)	76 (48%)
	Statistical error (p value)		7 (0.058)	46 (<0.0001)	39 (<0.0001)
	R^2 (p value)		0.83(<0.0001)	0.62 (0.0001)	0.77 (<0.0001)
	Adjusted R^2		0.82	0.60	0.76
Pooled 27 sub-regions	Mean (SD)	qCT	121 (55)		
		BP2E	119 (41)	151 (37)	139 (41)
	RMSE (%)		13 (3.7%)	155 (40%)	93 (14%)
	Statistical error (p value)		-2 (0.983)	30 (0.003)	18 (0.010)
	R^2 (p value)		0.71 (<0.0001)	0.37 (<0.0001)	0.32 (0.002)
	Adjusted R^2		0.70	0.36	0.31

Figure 1: FE model built from bi-planar dual energy (BP2E) and QCT images. The method to estimate the volumetric BMD (vBMD) distribution from BP2E images is detailed in the bolded grey square. First (1.), a vBMD distribution based on the QCT density database was used to build a generic distribution. Second (2.), a digitally reconstructed radiography (virtual aBMD image) was made based on the generic distribution from (1.). Third (3.) an iterative vBMD adjustment

was performed to maximize pixel similarity between the virtual and BP2E aBMD images. Once the image similarity was optimized, the personalized vBMD distribution from BP2E images was set.

Figure 2: Division of the vertebral body in 27 regions used to assess volumetric Bone Mineral Density distribution errors.

Figure 3: Error in the average vBMD distribution estimated from bi-planar dual energy (BP2E) X-ray absorptiometry radiographies compared to QCT images from the (A) the sagittal image alone, (B) the frontal image alone and (C) the sagittal and frontal images. Error in each of the 27 regions vBMD distribution estimated from the (D) the sagittal image alone, (E) the frontal image alone and (F) the sagittal and frontal images.

Figure 4: A) Regression Analysis and B) Bland and Altman plot between vertebral strength determined from BP2E-based FEM and qCT-based FEM. VBMD distribution estimated from the sagittal image only.

Figure1

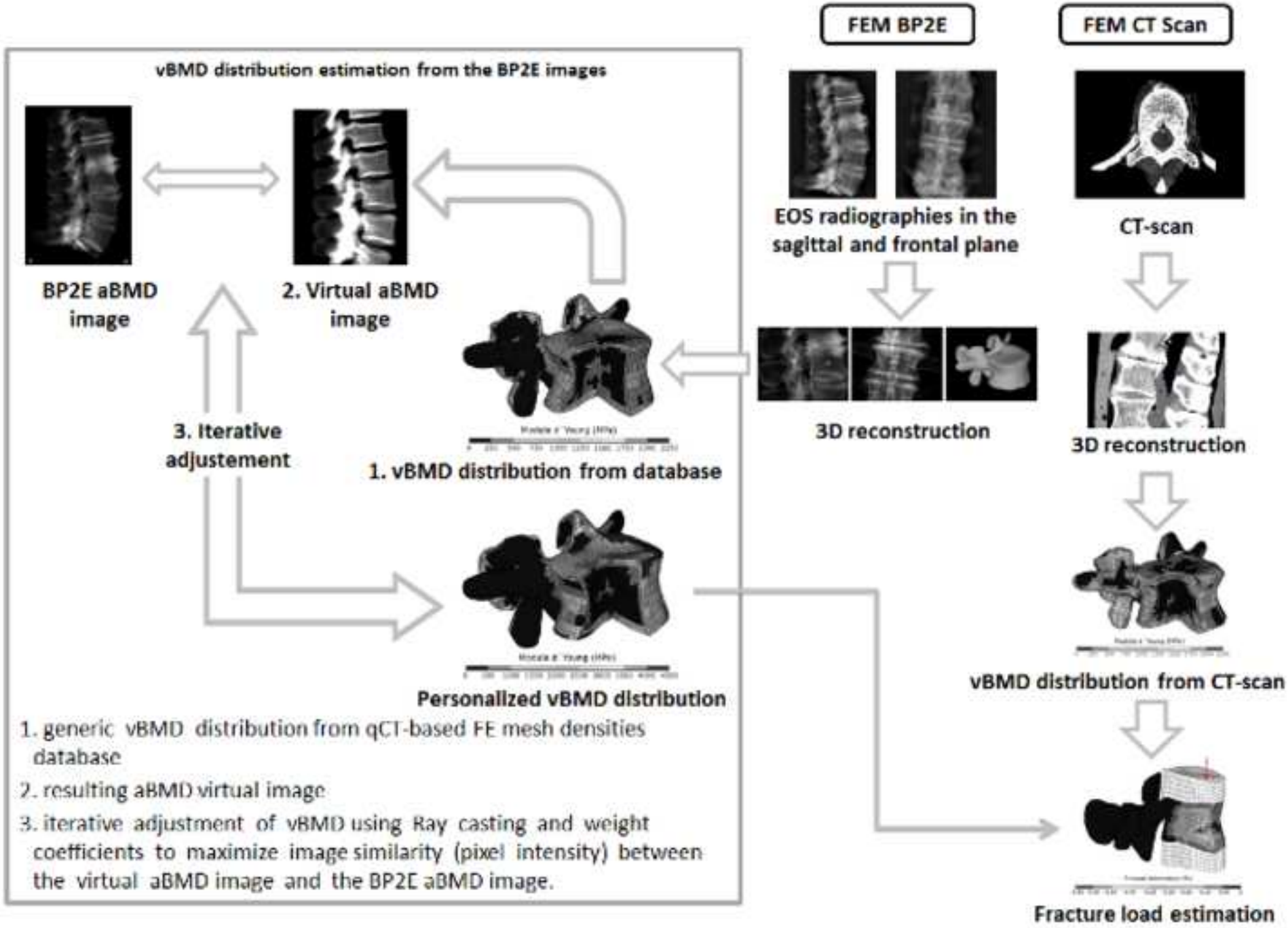
FEM BP2E
FEM CT Scan
vBMD distribution estimation from the BP2E images
BP2E aBMD image
2. Virtual aBMD image
EOS radiographies in the sagittal and frontal plane
CT-scan
3. Iterative adjustement
1. vBMD distribution from database
3D reconstruction
3D reconstruction
Personalized vBMD distribution
vBMD distribution from CT-scan
1. generic vBMD distribution from qCT-based FE mesh densities database
2. resulting aBMD virtual image
3. iterative adjustment of vBMD using Ray casting and weight coefficients to maximize image similarity (pixel intensity) between the virtual aBMD image and the BP2E aBMD image.
Fracture load estimation

Figure2

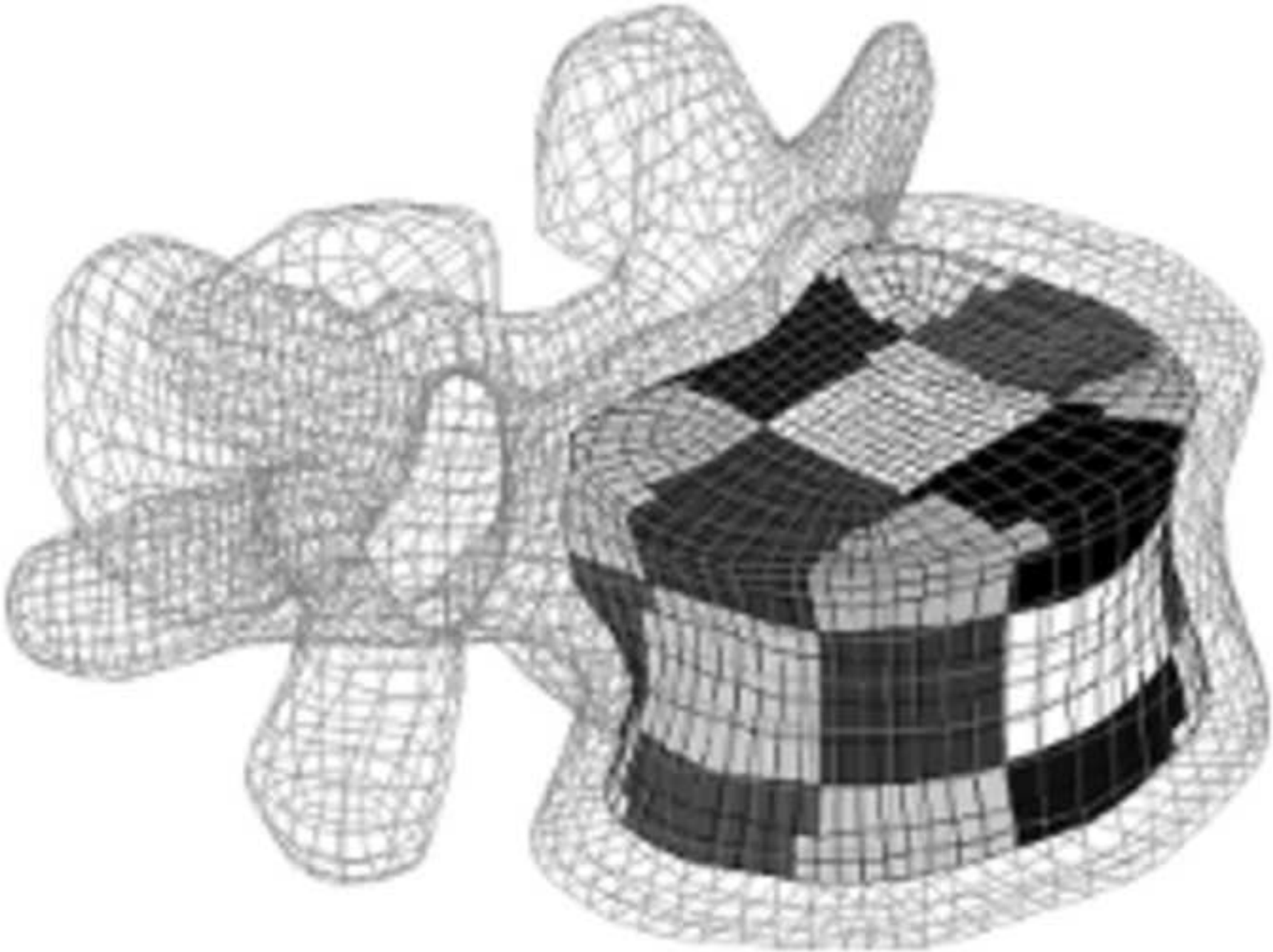

Figure3

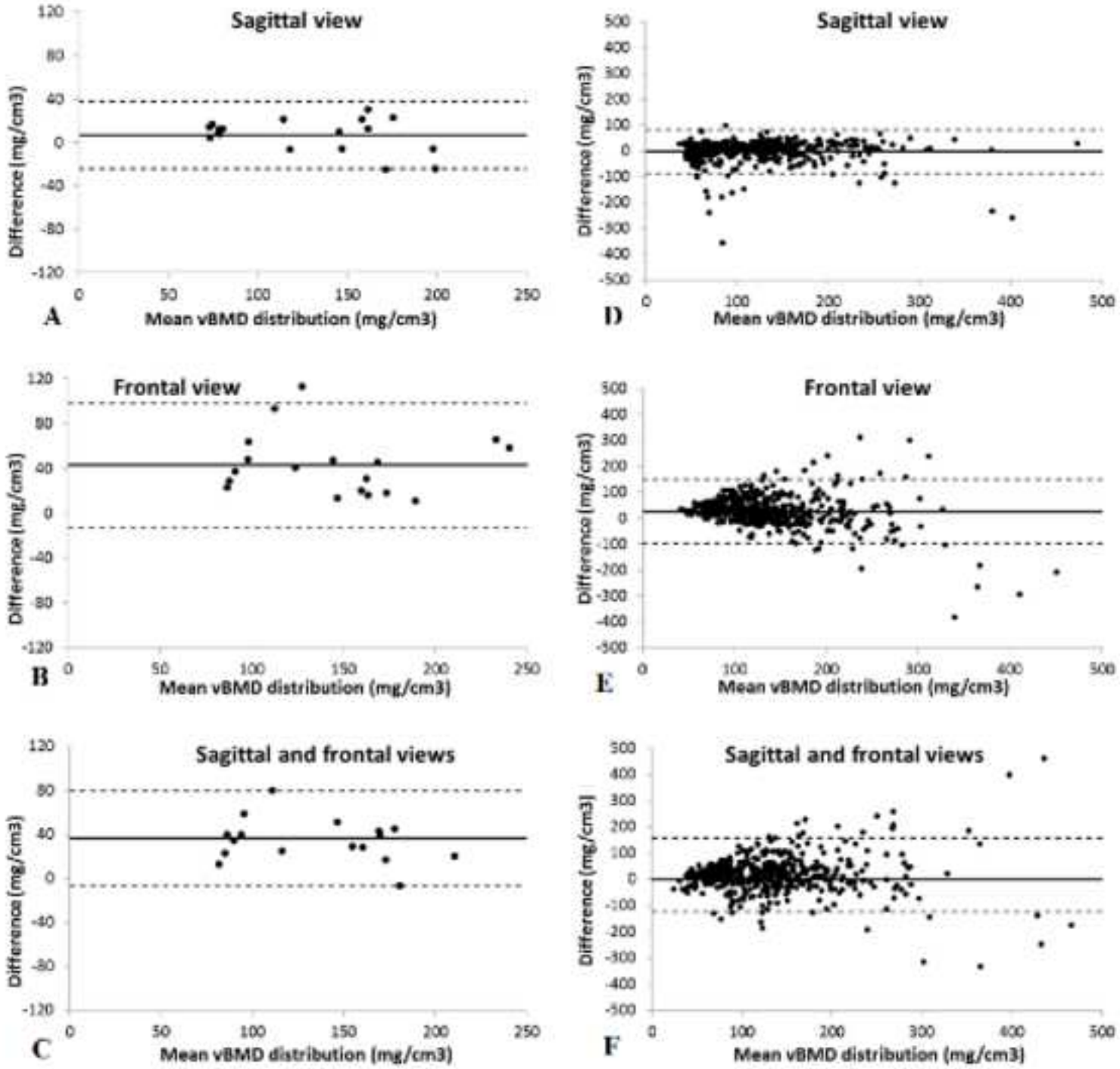
Sagittal view
Difference (mg/cm3)
Mean vBMD distribution (mg/cm3)
A
Sagittal view
Difference (mg/cm3)
Mean vBMD distribution (mg/cm3)
D
Frontal view
Difference (mg/cm3)
Mean vBMD distribution (mg/cm3)
B
Frontal view
Difference (mg/cm3)
Mean vBMD distribution (mg/cm3)
E
Sagittal and frontal views
Difference (mg/cm3)
Mean vBMD distribution (mg/cm3)
C
Sagittal and frontal views
Difference (mg/cm3)
Mean vBMD distribution (mg/cm3)
F

Figure4